Early speech and language outcomes in non-syndromic cleft palate with and without Robin Sequence: A matched case study

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ABSTRACT: Robin Sequence (RS) is a rare condition leading to orofacial anomalies, including cleft palate. Evidence suggests children with RS have poor long-term speech and language outcomes, even in comparison to those with isolated cleft palate. This study compared speech and language outcomes of children with isolated cleft palate (ICP) to children with cleft palate and RS (CPRS). A retrospective case-note review was completed of 74 matched children (37 ICP; 37 CPRS). Speech and language assessment at 18-months, three and five years provided data for palatal function and articulation. At age five years, children with CPRS had significantly more frequent and severe articulation errors than children with ICP. Palatal function across the two groups was not significantly different. Expressive and receptive language at three years did not differ. Results support previous studies highlighting the severity and frequency of articulation errors associated with CPRS. Further longitudinal investigation into language outcomes is recommended.

Key words: *Robin Sequence, cleft palate, speech, articulation, velopharyngeal insufficiency*

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Introduction

Robin Sequence (RS) is a congenital condition which occurs from 1 in 5600 to 1 in 30,000 children (Paes, van Nunen, Bassert & Breugem, 2015; Caouette-Laberge, Bayet & Larocque, 1994). It is heterogeneous, with an often-differing developmental prognosis across individuals (Thouvenin et al., 2013). In 2016, Breugem et al. produced a clinical consensus report regarding the characteristics of RS; micrognathia (small lower jaw) was determined the primary and initiating characteristic, with glossoptosis (retraction of the tongue) and airway obstruction cited as mandatory diagnostic characteristics. Although not included in the diagnostic criteria, cleft palate is most commonly Stickler's Syndrome[1] and 22q11 deletion syndrome[2] (Izumi et al, 2012).

Children with cleft palate and RS (CPRS) and children with cleft palate only, termed isolated cleft palate (ICP) in this paper, often require support to aid their speech and language development and commonly follow the same treatment pathway. Current evidence suggests that children with CPRS have increased speech and language difficulties when compared to

[1] Stickler syndrome is a disorder characterised by a distinctive facial appearance, hearing loss, joint problems and eye abnormalities.

[2] 22q11 deletion syndrome, also termed DiGeorge syndrome, is caused by the deletion of a segment of chromosome 22. Symptoms of 22q11 deletion syndrome often include congenital heart problems, developmental delay, learning difficulties and cleft palate or velopharyngeal incompetence.

children with ICP, but studies are sparse and often have samples including syndromic and non-syndromic RS (Filip et al., 2015; Thouvenin et al., 2013). Speech difficulties related to cleft palate include ongoing issues with palatal function resulting in velopharyngeal insufficiency (VPI). This leads to hypernasal resonance and nasal airflow errors accompanying consonant production. Compensatory and obligatory articulation errors can also develop. These are often referred to as Cleft Speech Characteristics (CSCs). These include anterior errors (e.g. lateral and palatal placement); posterior errors (e.g. backing to velar or uvular); non-oral errors (e.g. active nasal fricatives, glottal or pharyngeal placement); and passive errors (e.g. weak or nasalised errors related to ongoing structural difficulties with the velopharyngeal mechanism) (John, Sell, Harding-Bell, Sweeney & Williams, 2006).

Velopharyngeal insufficiency

Velopharyngeal Insufficiency (VPI) often occurs after repair of the cleft palate (Goudy, Ingraham & Canady, 2011) and some studies suggest that children with CPRS experience increased VPI. In a longitudinal prospective study, Thouvenin et al. (2013) assessed the speech of 39 children with RS (27 with isolated RS and 12 with RS and Stickler's syndrome) at 15 months and at three and six years. They analysed the long-term developmental outcomes of the children; at six-years 69% (N=25) had persistent hypernasal speech. In parity with this study, Filip et al. (2015) investigated a total of 93 non-syndromic individuals with CPRS over a 33-year period, collecting data retrospectively and comparing it with a large control group. After cleft palate repair 30 of 87 (34.5%) participants with non-syndromic and syndromic RS developed normal speech while 33.3% of 93 non-syndromic patients had surgery for VPI. This is a significantly higher rate when compared to the control group of individuals with ICP, of which only 19.4% received further surgery. Hardwicke, Richards, Cafferky, Underwood, ter Horst and Slator (2016) assessed articulation and nasality outcomes of 24 patients with RS at five years of age. These outcomes were compared with an ICP control group. Hardwicke et al. (2016) report that the RS group had significantly higher rates of secondary surgery (p=0.017) and significantly poorer nasality scores (p=0.031) than the ICP group. In another retrospective study of 130 children with isolated or syndromic CPRS, Morice et al. (2018) found similar rates of VPI (30.5%) in their isolated CPRS group at a mean age of 3.4 years.

Findings are mixed regarding VPI outcomes and not all studies report significant differences when comparing children with CPRS to children with ICP. Goudy, Ingraham and Canady (2011) state that children with RS do not have a higher rate of VPI after cleft palate repair and that they are no more likely to require additional surgery than children with ICP. However, in 2021, Schwaiger et al. produced the largest study reporting speech outcomes using an established standardised assessment tool within a follow-up time frame, comparing 51 patients with CPRS to an ICP cohort at age five years. They found that children with CPRS were more likely to need further surgery to correct VPI before age five years (p=0.016). In a systematic review by Wan et al. (2015), only six papers were found comparing the speech outcomes of children with RS compared to ICP. Four of the papers which measured VPI reported no significant outcomes. Meanwhile, Stranksy et al. (2013) found a significant difference in VPI between children with RS and those with ICP at age eight (p=0.04).

Articulation

Current research has compared articulation outcomes of children with CPRS, although often in small samples. In Wan et al.'s (2015) systematic review, only three papers studied articulation outcomes (Stranksy et al, 2013; Lehman, Fishman & Neiman, 1995; Khosla, Mabry & Castiglione, 2008). Their descriptions of error types were limited, and no significant group differences were found. In a matched comparison study of 24 children with RS and 24 with ICP, Hardwicke et al. (2016) found that the RS group had poorer articulation outcomes; they had significantly worse cleft speech characteristics (CSCs) (p=0.023) and produced more backed to velar errors, glottal substitutions and active nasal fricatives than the ICP group. The number of each CSC type found were not provided within the paper and only 24 participants were included in the study. In the larger Schwaiger et al. (2021) paper children with RS presented with a significantly higher rate of CSCs (p=0.001). Overall, the small number of papers, and the small sample sizes within the studies limits the application of results to clinical practice. Therefore, results are tentative, but do suggest that articulation outcomes at the age of five years after cleft palate repair were poorer in children with RS than for children with ICP.

Language difficulties

Children with cleft palate often perform poorly on assessments of language compared to their peers. A recent scoping review concluded that there is evidence of early language delay in children born with cleft lip and palate (van Eeden & Stringer, 2020). However, research investigating the language difficulties of children with RS/CPRS is scarce, and the existing literature has conflicting outcomes. One study by Smith et al. (2014) explored the outcomes related to sleep disturbance caused by obstructive sleep apnoea in children with CPRS at three years of age. Significant differences were found for both receptive (p=0.01) and expressive language (p=0.001) using the Bayley Scales of Infant and Toddler Development – III[3] (Bayley, 2006) when compared to children with ICP. Alencar et al. (2017) investigated 62 children with isolated RS and cleft palate, exploring whether airway management by positioning or nasopharyngeal airway tube affected rates of hypoxia which may lead to cognitive difficulties. They found that between 18.4% and 20.8% of children with CPRS were at risk of language difficulties. The Thouvenin et al. (2013) study discussed above, also analysed the long-term developmental outcomes of the children. At 15 months of age, the language scores for the children were below average, and at three years of age, 18 children (46%) still had language delay and their mean score on vocabulary subtest was below one standard deviation. However, no follow-up scores at six-years were reported.

Purpose of this study

There are limited longitudinal data regarding speech and language development in children with CPRS making it difficult to understand the speech and language difficulties of this population. Not enough is known about children with CPRS and how they differ from children with ICP. Research outcomes lack consensus with largely mixed results regarding speech and language outcomes. Further research is

[3] The Bayley Scales of Toddler Development is an assessment that is used to measure five areas of child development including cognition, motor skills, language, social-emotional abilities and adaptive behaviour.

necessary to better understand the treatment and management required by children with CPRS for successful speech and language development. Comparing children with CPRS to those with ICP in further investigations will increase our understanding of speech and language development for children with RS. The present study adds to the current evidence base by comparing the early speech and language outcomes of children with CPRS to a matched group of children with ICP, with the aim of informing clinical practice, enabling clinicians to identify which children are at risk of later speech and language difficulties.

Research Questions

This study aimed to answer the following questions:

Compared to non-syndromic children with isolated cleft palate, do children with non-syndromic Robin Sequence have:

1. Worse speech outcomes at five years in terms of velopharyngeal function and CSCs present in their articulation?

2. Worse early speech and language outcomes at 18 months and three years?

Secondary research questions explored correlations of speech outcomes with severity of cleft; presence of fistula post-surgery; history of hearing difficulties; expressive language at three years; receptive language at three years.

Ethical approval

Ethical approval was granted through the Newcastle University Education, Communication and Language Sciences ethics committee (REF. ECLS_317). NHS approvals in line with Caldicott principles were granted by Newcastle upon Tyne Hospitals NHS Foundation Trust (REF. NUTH/7141).

Method

Design

This was a retrospective, longitudinal, matched case study. Participants were taken from the caseload of a regional cleft lip and palate service in the United Kingdom. They were matched by socioeconomic status, gender and age at final speech assessment.

Table 1. Sample comparisons across the matched groups

Group	Mean (SD) age at final speech assessment (months)	Socioeconomic status (Mean IMD (SD))	Gender ratio (M:F)
Isolated Cleft Palate	64 (2.24)	4.03 (2.87)	17:20
Cleft Palate + Robin Sequence	65 (2.11)	4.43, (2.26)	16:21
Chi-square analysis	X^2 (10, N=74) = 7.71, p=.657	X^2 (8, N=74) = 9.15, p=.330	X^2 (1, N=74) = 0.55, p=.815; Fisher's Exact (2-sided) p=.100

Participants

All participants were born between 01/01/2004 and 31/12/2013. All had surgery carried out by a single surgeon. Chi-squared analysis confirmed group comparability (see Table 1). There was a total of 74 participants with 37 in each group.

Data collection

All data was stored electronically on a spreadsheet before being entered into IBM SPSS Statistics (IBM, 2016).

Primary outcome measures

Data from a five year audit assessment regarding velopharyngeal function and CSCs was collected following the Cleft Audit Protocol for Speech–Augmented (CAPS-A) protocol (John et al., 2006). The CAPS-A is used throughout the United Kingdom to audit speech outcomes at five-years and is a robust measure of velopharyngeal function and articulation outcomes derived through intense training of speech and language therapists (SLTs), with ongoing calibration and a consensus listening process (Sell et al. 2009). Data included measures of resonance, nasal airflow and the presence of anterior, posterior, non-oral or passive CSCs.

Secondary outcome measures

Data identifying rates of secondary surgery was collected. Early speech and language data were also investigated. Data on resonance and presences of CSCs at 18 months and three years were collected from the speech and language records along with data from language assessments collected at three years. This was taken from informal observation and spontaneous speech samples using methods described in the Derbyshire Language Scheme (Knowles &

Masidlover, 1982). For example, understanding at one-word level was rated as a severe delay at three-years, whilst understanding of three or more information-carrying words in an instruction was considered as normal for their age. The equivalent was used for expressive language; an expressive level of only single words at age three was regarded as a severe delay.

Confounding variables

The following data were collected from medical records to investigate any associations with the primary outcome measures and confounding variables: severity of the cleft; age at primary palate repair, history of fistulae following surgery; hearing history.

Data analysis

IBM SPSS Statistics for Windows, Version 21.0was used for all data analysis. Data on resonance, nasal airflow and non-oral CSCs were combined using the VPC-SUM method described in Lohmander et al., 2017. This is calculated on a 3-point scale to describe velopharyngeal function (0 = competent, 1 = borderline, 2 = incompetent). Data on CSCs were collated into seven levels in order of severity – none, anterior, posterior, non-oral, anterior and posterior, anterior and non-oral, all three types. Frequency statistics were obtained for speech and language outcomes at 18 months, 3 years and 5 years, as well as secondary surgery, fistulae rates and hearing history. Group differences were analysed using a non-parametric Mann-Whitney U test, using a p-value of <0.05 as level of significance. Correlations, using Spearman's Rho (one-tailed), were made to investigate the associations of identified early risk factors with the primary outcomes; these were the secondary outcomes and confounders outlined above. Further inferential statistics using binary logistic regression were carried out to analyse the extent to which poor speech outcomes could predict to which group a participant belonged.

Results

Primary outcome measures

Speech results at five years were taken as the primary outcome measure, as reported by consensus among specialist SLTs working in the field of cleft palate and velopharyngeal dysfunction.

For velopharyngeal function, 76% of the CPRS group had competent VP function compared with 92% of the ICP group. This difference was not statistically significant (p=.055). However, a weak, significant negative correlation was seen between velopharyngeal function at five years and whether a child was in the CPRS or ICP group (r=-.225, p=.027), meaning that there was an association between a diagnosis of RS and the likelihood of ongoing VPI. Binary logistic regression analysis showed that poor velopharyngeal function at five years did not significantly predict whether a participant had a diagnosis or RS or not (B=.786, Exp(B)=2.195, p=.106). For articulation, only 32% of the CPRS group had good articulation with no evidence of CSCs at age five; this compared to 65% of the ICP group and was found to be highly significant (p=.002). A weak to moderate negative correlation was seen between articulation at five years and whether a child was in the CPRS or ICP group (r=-.367, p=.001), meaning that there was an association between a diagnosis of RS and significant articulation difficulties. Binary logistic regression showed that an increased level of articulation difficulty made it more likely a participant had a diagnosis of RS (B=.472, Exp(B)=1.602, p=.018).

Secondary outcome measures

For secondary surgery, a total of 8 children had had secondary surgery for speech by the time of their five year speech assessment. There were 6 in the RS group (16%) and 2 in the ICP group (5%). This did not represent a significant difference (Fishers Exact 2-sided, p=.261). For language scores, language measures were only available at 3-years. Language samples from which to gather speech development data at 18-months differed between the groups, with only 41% of the CPRS group with enough language at this age compared with 59% of the ICP group. For expressive language skills, 46% of the CPRS group were considered to be delayed, compared with 38% of the ICP group. This difference was not statistically significant (Fisher's Exact 2-sided, p=.621). For receptive language skills, 43% of the CPRS group were considered to have a delay, compared with 31% of the ICP group. Again, this was not statistically significant (Fisher's Exact 2-sided, p=.449). Although there were no significant differences seen between groups, there was a weak positive correlation with articulation at five years and both expressive language (r=.243, p=.024) and receptive language (r=.281, p=.011) at three years. This means there was an association between poorer language skills at age three years and articulation difficulties at five years.

Confounding variables

Regarding severity of the cleft, there was a significant difference across the groups in terms of the type of cleft palate; 97% of the CPRS group had a cleft of the hard and soft palate compared with only 54% of the ICP group (p<.001). For age at palate repair, there was a significant difference in the range of ages at which palates were repaired with the majority of those in the CPRS group being repaired at around 12-months and those in the ICP group at 6-months (p=.006). With presence of a fistula after primary repair, there was a significant difference across groups with regard to fistulae with 32% of the CPRS group having a fistula after primary repair compared to 8% of the ICP group (p=.018). As for history of hearing problems, no significant group differences were seen here; 68% of the CPRS group had a history of hearing problems compared to 62% of the ICP group (p=.603). Weak to moderate significant correlations were seen between velopharyngeal function at five years and post-surgical fistulae (r=.329, p=.006) and severity of the cleft (r=.248, p=.033). Weak to moderate significant correlations were seen between articulation at five years and post-surgical fistulae (r=.388, p=.001), severity of the cleft (r=.365, p=.001) and hearing difficulties (r=.258, p=.033). The binary logistic regression showed that of the confounding variables, only the severity of the cleft palate was found to be significant when adjusting for the influence of both velopharyngeal function at five years (B=3.346, Exp(B)=28.379, p=.002) and articulation at five years (B=.3.173, Exp(B)=23.876, p=.004) on group membership.

Longitudinal data

Speech data was collected at 18-months, three years and five years in order to observe patterns of development between the two groups. At all ages the CPRS group had poorer outcomes.

Velopharyngeal function - At 18 months of age only 15 of the children in the CPRS group had a large enough spontaneous language sample to assess VP function, compared with 22 in the ICP group. All those that had samples to analyse were rated as having competent VP function using the VPC-SUM. At 3 years, 73% of

the children in the CPRS group had competent VP function, compared to 94% in the ICP group. This was found to be a significant difference (p=.029). As reported above, by five years the gap had closed a little to 76% of the CPRS group having competent VP function compared with 92% of the ICP group and was no longer a significant difference (p=.055). See Figure 1. At 18 months of age 60% of the children in the CPRS group were not showing signs of developing CSCs in their speech; this compared with 100% in the ICP group. This was highly significant (p=.001). At 3 years, only 53% of the children in the CPRS group had good articulation with no CSCs, compared to 73% in the ICP group. By this age the group differences seen were non-significant (p=.053). But as reported above, by five years the rates of CSCs had increased in both groups and the gap had widened again with only 32% of the CPRS group having good articulation with no CSCs, compared with 65% of the ICP group (p=.002). See Figure 2 for further breakdown of the types of CSCs reported at the different ages

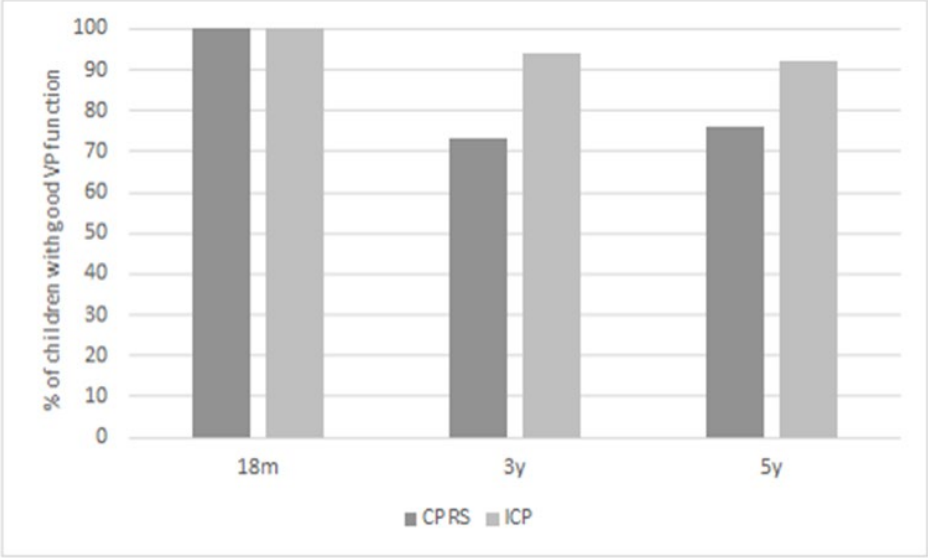

Figure 1. Longitudinal data regarding velopharyngeal function

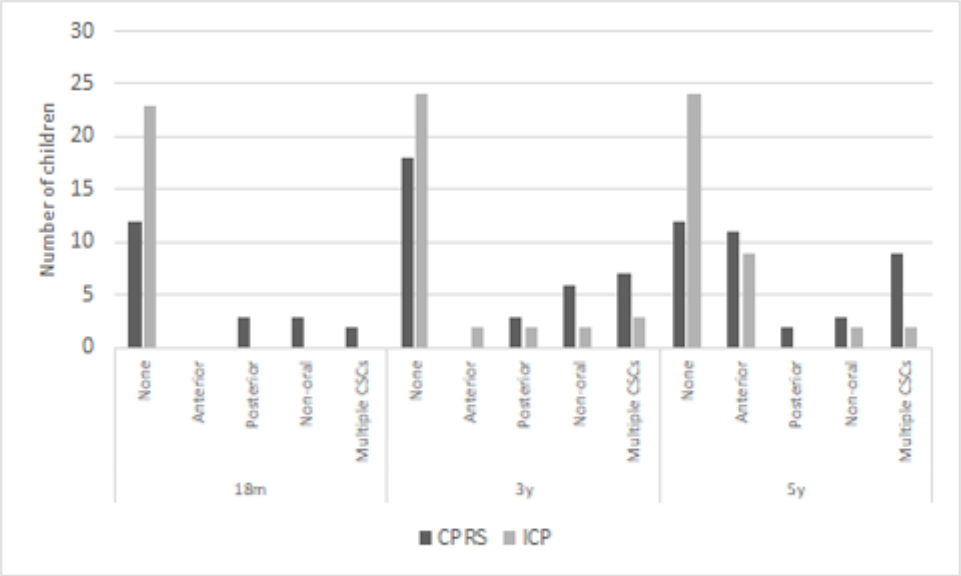

Figure 2. Longitudinal data for articulation and breakdown of CSCs

Across all the ages studied, the CPRS group had poorer outcomes, with the gap between this group and peers with ICP widening for articulation skills as they reached five years.

Discussion

In the present study, speech outcomes at the age of five years after cleft palate repair were poorer in children with CPRS than for children in the matched ICP comparison group. The CPRS group performed significantly worse in terms of articulation. Comparison can be made between the present study and results published by Hardwicke et al. (2016) and Schwaiger et al. (2021). All three studies had comparable surgical protocols and used the same validated speech assessment tool (John et al., 2006). Consistent with the present study, both Hardwicke et al. (2016) and Schwaiger et al. (2021) found statistically significant differences in CSCs between CPRS and ICP cohorts, reporting that CPRS participants performed worse than their ICP counterparts.

Palatal function at age 5-years between the two groups was not significantly different in the present study, which is in harmony with recent reports (Schwaiger et al., 2021). Overall, more children with CPRS had VPI than the ICP group; 24% of children with CPRS presented with mild or severe VPI, which is slightly below recently reported VPI rates for non-syndromic CPRS by Morice et al. (2018) (30.5%), Stransky et al. (2013) (47%) and Hardwicke et al. (2016) (46%). Interestingly, prior studies have shown mixed results when comparing VPI outcomes in children with CPRS to children with ICP. Thouvenin et al. (2013)'s longitudinal study involved a similar sample size, to the present study yet included syndromic cases of CPRS. Nevertheless, they found contrasting outcomes. At the age of six years, children with CPRS had significantly increased VPI compared to children with ICP (Thouvenin et al, 2013). Several additional studies comparing CPRS with ICP support this conclusion (Goudy, Ingraham & Canady, 2011; Khosla, Mabry & Castiglione, 2008; Hardwicke et al., 2016; Morice et al., 2018). It is however unclear from these studies whether any secondary surgery for speech had taken place. In this study six children in the CPRS group had already had secondary surgery by the age of five which influenced the velopharyngeal function outcome.

Expressive and receptive language outcomes at three years did not differ significantly between the CPRS and ICP groups. These outcomes add to the discussion regarding language difficulties in RS, although results remain limited. Though not found in the present study, significant differences for both receptive and expressive language have been reported in recent years when comparing children with RS to those with ICP (Smith et al., 2014). In a longitudinal study, Thouvenin et al. (2013) found that 18 of 39 children with RS still had language delay at age three years. However, 12 of the 39 children within Thouvenin et al.'s (2013) study had RS associated with Stickler's syndrome. In the present study, children with CPRS and associated syndromes were excluded, which could account for the differences in results. Whilst a significant difference between the ICP and CPRS groups was not observed in this study, more children with CPRS did have language difficulties, at a rate comparable to that in the Thouvenin et al. study (46% at three years). Therefore, it could be postulated that children with CPRS have more language difficulties than children with ICP and that this was not detected statistically due to methodological consequences. For example, there is potential that the language outcomes reported in the present study were

impacted by the assessments used within the service. There is reason to believe that the language assessments used may not have been sensitive enough to detect a difference in difficulties between the two groups; decisions regarding language were based on spontaneous speech samples using a non-standardised measure which may not have captured subtle but important differences in the children's abilities. Moreover, it is important to note that language data for some participants was missing, meaning language results were not representative of the whole cohort. Whilst this notion regarding language results is not entirely without substance, it may be a result of researcher bias linked to preconceptions of previous literature and study expectations. Overall, language outcomes from this study are tentative and must be considered with caution. Further investigation and longitudinal follow-up are warranted to explore whether language results were impacted by the assessment used and the absence of data.

Strengths and Limitations

Comparison groups have been used previously in research. Studies have compared syndromic versus non-syndromic RS cohorts (Wagener 2003; de Buys 2008; Witt 1997). In addition, comparisons have been made between non-RS cohorts and RS cohorts both matched and unmatched (Stranksy, 2013; Goudy, Ingraham & Canady, 2011; Lehman, Fishma & Neima, 1995), not dissimilar to the present study. The sample size achieved within this study (37 in each group), although larger than existing studies (Hardwicke et al., 2016; Schwaiger et al., 2021), remains relatively small. Goudy et al. (2011) suggest that matching by age, sex, age at primary surgery and cleft anatomy forms a valuable comparison group; participants with CPRS were matched in terms of socio-economic status, gender, date of birth and age at 5-year speech audit, which strengthens the group comparison. Moreover, age at primary surgery was accounted for in the regression analysis and was not found to significantly contribute to the outcomes. However, the severity of the cleft was found to significantly influence the outcomes for both groups. It is not possible to tell from this study whether the diagnosis of RS contributes to poorer speech outcomes or whether the severity of the cleft has a greater influence. Future studies should ensure that groups are matched by severity of the cleft.

Prior findings suggests that there would be a much higher rate of syndromic CPRS patients if they were genetically screened (Izumi et al, 2012). Although none of the participants in the present study had a diagnosed syndrome, it is acknowledged that there may be participants with undiagnosed syndromes within the ICP and/or CPRS groups, which could have impacted study results. Contrasting outcomes have been found comparing syndromic versus non-syndromic RS patients. No statistically significant differences in speech outcomes between syndromic and non-syndromic RS patients were observed in Schwaiger et al.'s 2021 case series whereas Patel et al. (2012) and more recently Logjes et al. (2021) report significantly worse speech outcomes in syndromic RS patients.

Most prior comparative studies have been retrospective and completed within single establishments, which is the case for the present study. The retrospective nature meant that recordkeeping could not be controlled, and treatment fidelity could not be promoted. Whether participants received intervention or support over the years monitored was not included, which could have impacted speech and language outcomes. As information was gathered from case files retrospectively, participants were excluded because their

five year speech audit was missing or incomplete. This occurred in prior studies (Hardwicke et al., 2016) and could be deemed an element of selection bias.

Conclusion

This study highlights the severity of cleft speech characteristics in children with Robin Sequence. Children with CPRS experience worse articulation outcomes when compared to children with ICP, and likely require increased support in this area. In agreement with prior research, results demonstrate the vulnerability of this client group. Too little evidence exists regarding this rare congenital condition in terms of speech and especially language outcomes. There is a need for large scale multi-disciplinary studies to allow for the development of specific standards and processes to support children with RS.

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